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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,673	06/03/2002	Howard Green	H0535/7014	6874

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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,673	GREEN ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,24,36,51,95-104 and 106-118* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 24, 36, 51, 95-104 and 106-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and reply filed 2/27/06 are acknowledged. Claim 105 has been cancelled and new claims 112-118 have been added.

Claims 1-10, 24, 36, 51, 95-104 and 106-118 are under examination.

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/359,987, filed 7/22/1999. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications.

Claim Rejections - 35 USC § 102

Claim 36 stands rejected under 35 U.S.C. 102(b) as being clearly anticipated by Urry (US 4,589,882; cited in previous Office action).

Applicant argues that the amendment to claim 36 overcomes the rejection.

Claim 36 has been amended to recite that the agent is a conjugate of an active agent attached to a linker not native to the active agent. Urry meets this limitation. Urry teaches that the bioelastomeric polypeptides can be bonded to a material that imparts strength to the elastic fibers. The bioelastomeric polypeptide is chemically bonded to a collagen fiber of core analog (col. 11, lines 14-56). Thus, the bioelastomeric polypeptides function as the linker and the agent is the collagen strengthening fiber. The bioelastomeric polypeptide is not native to the collagen fiber. Thus, Urry meets the newly added limitation.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 36, 106, 107, and 115-117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 117 are rejected because it is unclear at what time in an active agent's life that a linker is considered to be native or not native. "Nativity" is relative to time that a molecule is observed. One can observe a molecule but not know what, if anything, has been added or subtracted from it.

Claim 106 is rejected because it fails to further limit claim 36. It would seem that the "native active agent" of claim 106 is redundant. Presumably the active agent of claim 36 is native.

Claims 115 and 116 are rejected because they fail to further limit claim 114. It would seem that the "native active agent" of claims 115 and 116 is redundant. Presumably the active agent of claim 114 is native.

Claim Rejections - 35 USC § 103

Claims 1-3, 36, 98-101, and 118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richardson et al. (US 5,490,980) in view of Stedronsky (US 6,258,872; cited in previous Office action) and Urry (US 4,589,882).

Richardson et al. disclose a method for attaching an alkylamine-modified bioactive agents to skin, hair or nails via transglutaminase cross-linking. The alkylamine is -RNH_2, wherein R is 1 to 8 carbons, unbranched. The alkylamine is chemically bonded to the active agent such the amine is free to cross-link with the proteins in the human tissue. The bioactive agent includes antimicrobials, skin or hair conditioning agents, coloring agents, antioxidants, perfumes, proteins and the like (col. 2, lines 44-68 to col. 3). Richardson et al. also disclose that the alkylamine linker can be attached to fluorescent microspheres (i.e. microparticles). The amine-modified microspheres were attached to hair via

crosslinking by TGase (Ex. 5, col. 18). Richardson et al. does not teach a particular order of addition of the amine-modified agent and the TGase.

Richardson et al. do not teach the employment of lysine oxidase instead of TGase for cross-linking the alkylamine-modified agents to human tissue.

Stedronsky discloses a method for enhancing the mechanical performance of tissue adhesives and sealants (referred to as adhesive/sealant) in damaged tissue by inserting a primer molecule between said tissue and the adhesive/sealant which is a protein or synthetic polymer (col. 7, lines 11-27). The adhesive/sealant is crosslinked by covalent or non-covalent means. Covalent means include enzymatic cross-linking by any of the following enzymes: is lysyl oxidase, a transglutaminase, a phosphorylase, a glycosylase or a fatty acetyltransferase (col. 8, lines 33-41). The order of addition of the primer, adhesive/sealant and the crosslinker to the body tissue can vary. The tissue adhesive/sealant and the primer can be applied to the tissue and then cross-linked by the enzyme. The primer and the adhesive/sealant can be combined and applied to the tissue followed by cross-linking (col. 8, lines 51-68).

Urry discloses the application of bioelastic polymers to tissue to the repair of damage to said tissue. The polymers are natural substrates of lysyl oxidase which is naturally occurring in tissue. The lysyl oxidase present in the tissue effect the cross-linking of the bioelastomeric polypeptides and the tissue (col. 7, lines 25-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ lysine oxidase as the crosslinker instead of TGase in the invention of Richardson et al. The ordinary artisan would have been motivated to do so because lysine oxidase serves the same purpose as TGase since it crosslinks polymers, especially proteins to body tissue. The ordinary artisan would have had a reasonable expectation that lysine oxidase would successfully serve as a crosslinker in the invention taught by Richardson et al. because Urry teaches that lysine oxidase is a naturally occurring enzyme in human tissues that is responsible for crosslinking biopolymers in human tissue as well as

bioelastomeric polymers to human tissue. Additionally, Stedronsky discloses that lysine oxidase and transglutaminase are both suitable tissue/agent cross-linking enzymes.

Double Patenting

Claims 1-10, 24, 36, 51, 95-104 and 108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-46 and 48 of U.S. Patent No. 6,267,957 in view of Stedronsky (US 6,258,872), Urry (US 4,589,882), and Webster's Dictionary (p. 857; cited in the previous Office action).

The claims of '957 are drawn to a method for attaching a non-corneocyte protein, an agent, to a body comprising conjugating the agent to a carboxamide -containing linking molecule and then attaching he linked agent to the body tissue via transglutaminase. The claims meet the limitation in the instant application regarding the term "microparticle" because a microparticle is interpreted as a small part (as defined by Webster's Dictionary: a "particle" is a tiny piece or part (p. 857) and non-corneocyte proteins are small parts of matter. '957 does not claim the employment of lysine oxidase to effect the crosslinking reactions.

Stedronsky discloses a method for enhancing the mechanical performance of tissue adhesives and sealants (referred to as adhesive/sealant) in damaged tissue by inserting a primer molecule between said tissue and the adhesive/sealant. The adhesive/sealant is crosslinked by covalent or non-covalent means. Covalent means include enzymatic cross-linking by any of the following enzymes: is lysyl oxidase, a transglutaminase, a phosphorylase, a glycosylase or a fatty acetyltransferase (col. 8, lines 33-41).

Urry discloses the application of bioelastic polymers to tissue to the repair of damage to said tissue. The polymers are natural substrates of lysyl oxidase which is naturally occurring in tissue. The lysyl oxidase present in the tissue effect the cross-linking of the bioelastomeric polypeptides and the tissue (col. 7, lines 25-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute lysine oxidase for transglutaminase in the invention of '957. The ordinary artisan would have been motivated to do so because lysine oxidase and transglutaminase are equivalent alternatives for cross-linking of biological agents and proteins. The ordinary artisan would have had a reasonable expectation that lysine oxidase would successfully serve as a cross-linking agent in the invention of '957 because Urry teaches that lysine oxidase is a naturally occurring enzyme in human tissues that is responsible for crosslinking biopolymers in human tissue as well as bioelastomeric polymers to human tissue. Additionally, Stedronsky discloses that lysine oxidase and transglutaminase are both suitable tissue/agent cross-linking enzymes.

Claims 1-10, 24, 36, 51, 95-104 and 106-118 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 of copending Application No. 11/144,372 in view of Stedronsky (US 6,258,872), Urry (US 4,589,882), and Webster's Dictionary (p. 857; cited in the previous Office action).

The claims of '372 are drawn to a method for attaching a non-corneocyte protein, an agent, to a body comprising conjugating the agent to a carboxamide -containing linking molecule and then attaching he linked agent to the body tissue via transglutaminase. The claims meet the limitation in the instant application regarding the term "microparticle" because a microparticle is interpreted as a small part (as defined by Webster's Dictionary: a "particle" is a tiny piece or part (p. 857)) and non-corneocyte proteins are small parts of matter. '372 does not claim the employment of lysine oxidase to effect the crosslinking reactions.

Stedronsky discloses a method for enhancing the mechanical performance of tissue adhesives and sealants (referred to as adhesive/sealant) in damaged tissue by inserting a primer molecule between said tissue and the adhesive/sealant. The adhesive/sealant is crosslinked by covalent or non-covalent means. Covalent means include enzymatic cross-linking by any of the following enzymes: is lysyl

oxidase, a transglutaminase, a phosphorylase, a glycosylase or a fatty acetyltransferase (col. 8, lines 33-41).

Urry discloses the application of bioelastic polymers to tissue to the repair of damage to said tissue. The polymers are natural substrates of lysyl oxidase which is naturally occurring in tissue. The lysyl oxidase present in the tissue effect the cross-linking of the bioelastomeric polypeptides and the tissue (col. 7, lines 25-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute lysine oxidase for transglutaminase in the invention of '372. The ordinary artisan would have been motivated to do so because lysine oxidase and transglutaminase are equivalent alternatives for cross-linking of biological agents and proteins. The ordinary artisan would have had a reasonable expectation that lysine oxidase would successfully serve as a cross-linking agent in the invention of '372 because Urry teaches that lysine oxidase is a naturally occurring enzyme in human tissues that is responsible for crosslinking biopolymers in human tissue as well as bioelastomeric polymers to human tissue. Additionally, Stedronsky discloses that lysine oxidase and transglutaminase are both suitable tissue/agent cross-linking enzymes.

This is a provisional obviousness-type double patenting rejection.

Claims 1-10, 24, 36, 51, 95-104 and 106-118 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-50 of copending Application No. 11/125,830 in view of Stedronsky (US 6,258,872) and Urry (US 4,589,882).

The claims of '830 are drawn to a method for attaching microparticles to the surface of the skin of a subject comprising conjugating microparticles to the skin via endogenous transglutaminase. '830 does not claim the employment of lysine oxidase, endogenously or exogenously, to effect the crosslinking reaction.

Stedronsky discloses a method for enhancing the mechanical performance of tissue adhesives and sealants (referred to as adhesive/sealant) in damaged tissue by inserting a primer molecule between said tissue and the adhesive/sealant. The adhesive/sealant is crosslinked by covalent or non-covalent means. Covalent means include enzymatic cross-linking by any of the following enzymes: is lysyl oxidase, a transglutaminase, a phosphorylase, a glycosylase or a fatty acetyltransferase (col. 8, lines 33-41).

Urry discloses the application of bioelastic polymers to tissue to the repair of damage to said tissue. The polymers are natural substrates of lysyl oxidase which is naturally occurring in tissue. The lysyl oxidase present in the tissue effect the cross-linking of the bioelastomeric polypeptides and the tissue (col. 7, lines 25-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute lysine oxidase for transglutaminase in the invention of '830. The ordinary artisan would have been motivated to do so because lysine oxidase and transglutaminase are equivalent alternatives for cross-linking of biological agents and proteins. The ordinary artisan would have had a reasonable expectation that lysine oxidase would successfully serve as a cross-linking agent in the invention of '830 because Urry teaches that lysine oxidase is a naturally occurring enzyme in human tissues that is responsible for crosslinking biopolymers in human tissue as well as bioelastomeric polymers to human tissue. Additionally, Stedronsky discloses that lysine oxidase and transglutaminase are both suitable tissue/agent cross-linking enzymes.

This is a provisional obviousness-type double patenting rejection.

Claims 1-10, 24, 36, 51, 95-104 and 106-118 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 25, 145-152, 155, 156, 158-165 and 167-173 of U.S. Patent 6,958,148 (Application No. 09/620,783) in view of Stedronsky (US 6,258,872) and Urry (US 4,589,882).

The claims of '148 are drawn to a method for attaching microparticles to the body tissue of a subject comprising conjugating microparticles to the tissue via endogenous or exogenous transglutaminase. The claims meet the limitation in the instant application regarding the term "agent" because a microparticle is an agent. '148 does not claim the employment of lysine oxidase, endogenously or exogenously, to effect the crosslinking reaction.

Stedronsky discloses a method for enhancing the mechanical performance of tissue adhesives and sealants (referred to as adhesive/sealant) in damaged tissue by inserting a primer molecule between said tissue and the adhesive/sealant. The adhesive/sealant is crosslinked by covalent or non-covalent means. Covalent means include enzymatic cross-linking by any of the following enzymes: is lysyl oxidase, a transglutaminase, a phosphorylase, a glycosylase or a fatty acetyltransferase (col. 8, lines 33-41).

Urry discloses the application of bioelastic polymers to tissue to the repair of damage to said tissue. The polymers are natural substrates of lysyl oxidase which is naturally occurring in tissue. The lysyl oxidase present in the tissue effect the cross-linking of the bioelastomeric polypeptides and the tissue (col. 7, lines 25-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute lysine oxidase for transglutaminase in the invention of '830. The ordinary artisan would have been motivated to do so because lysine oxidase and transglutaminase are equivalent alternatives for cross-linking of biological agents and proteins. The ordinary artisan would have had a reasonable expectation that lysine oxidase would successfully serve as a cross-linking agent in the invention of '830 because Urry teaches that lysine oxidase is a naturally occurring enzyme in human tissues that is responsible for crosslinking biopolymers in human tissue as well as bioelastomeric polymers to human tissue. Additionally, Stedronsky discloses that lysine oxidase and transglutaminase are both suitable tissue/agent cross-linking enzymes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
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